PATENT Axelsson and Good Atty Docket No.: INDEX1140-1

Application No.: 10/582,946 Filed: March 2, 2007

Page 2

## Amendments to the Claims

Please amend claims 1, 4, 5 and 13-16 as indicated in the listing of claims.

Please cancel claims 2, 6 and 25 without prejudice or disclaimer.

The listing of claims will replace all prior versions, and listings of claims in the application.

## **Listing of Claims:**

- 1. (Currently Amended) A short interfering RNA (siRNA) molecule that down regulates expression of a p65 subunit of NF-kappa-B gene by RNA interference, said siRNA molecule comprising a sense region and an antisense region and wherein said antisense region comprises a sequence complementary to an RNA sequence encoding the p65 subunit of NF-kappa-B and the sense region comprises a sequence complementary to the antisense region, wherein said antisense region comprises consists of a sequence substantially complementary to a sequence selected from the group consisting of SEQ ID NO: 1, 2, 3 and 4 and wherein said antisense region comprises a sequence selected from the group consisting consists of SEQ ID NO: 5, 6, and 8 or substantially homologous sequences thereof and said sense region consists of SEQ ID NO: 9.
- 2. (Canceled)
- 3. (Original) The siRNA molecule of claim 1, wherein said sense region and antisense region are covalently connected via a linker molecule.
- 4. (Currently amended) The siRNA molecule of claim + 3, wherein said linker molecule is a polynucleotide linker.
- 5. (Currently amended) The siRNA molecule of claim 4 3, wherein said linker molecule is a non-nucleotide linker.
- 6. (Canceled)

Axelsson and Good

Application No.: 10/582,946 Filed: March 2, 2007

Page 3

7. (Withdrawn) The siRNA molecule of claim 1, wherein said sense region comprises the sequence of SEQ ID NO: 10 and said antisense region comprises a sequence of SEQ ID NO: 6.

PATENT

Atty Docket No.: INDEX1140-1

- 8. (Withdrawn) The siRNA molecule of claim 1, wherein said sense region comprises the sequence of SEQ ID NO: 12 and said antisense region comprises the sequence of SEQ ID NO: 8.
- 9. (Previously presented) The siRNA molecule of claim 1, wherein said sense region comprises a 3'-terminal overhang and said antisense region comprises a 3'-terminal overhang.
- 10. (Previously presented) The siRNA molecule of claim 9, wherein said 3'-terminal overhang comprises 1 to 5 natural or modified nucleotides.
- 11. (Previously presented) The siRNA molecule of claim 9, wherein said antisense region 3'-terminal overhang is complementary to RNA encoding p65 subunit of NF-kappa-B.
- 12. (Original) The siRNA molecule of claim 1, wherein said sense region comprises one or more 2'-O-methyl modified pyrimidine nucleotides.
- 13. (Currently amended) The siRNA molecule of claim 1, wherein said sense strand region comprises a terminal cap moiety at the 5'-end, 3'-end, or both 5' and 3' ends of said sense region.
- 14. (Currently amended) The siRNA molecule of claim 1, wherein said antisense strand region comprises one or more 2'-deoxy-2'-fluoro modified pyrimidine nucleotides.
- 15. (Currently amended) The siRNA molecule of claim 1, wherein said antisense and/or sense strand region comprises between one and up to and including five phosphorothioate internucleotide linkages at the 3' end of said antisense and/or sense region.
- 16. (Currently amended) The siRNA molecule of claim 1, wherein said antisense and/or sense strand region comprises between one and up to and including five phosphorothioate internucleotide linkages at the 5' end of said antisense and/or sense region.

Axelsson and Good

Application No.: 10/582,946

Filed: March 2, 2007

Page 4

17. (Previously presented) The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhang comprises ribonucleotides that are chemically modified at a nucleic acid sugar, base, or backbone.

PATENT

Atty Docket No.: INDEX1140-1

- 18. (Previously presented) The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhang comprises deoxyribonucleotides that are chemically modified at a nucleic acid sugar, base, or backbone.
- 19. (Previously presented) The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhang comprises one or more universal base ribonucleotides.
- 20. (Previously presented) The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhang comprises one or more acyclic nucleotides.
- 21. (Previously presented) The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhang comprises nucleotides or non-nucleotides.
- 22. (Original) An expression vector comprising a nucleic acid sequence encoding at least one siRNA molecule of claim 1 in a manner that allows expression of the nucleic acid molecule.
- 23. (Original) A mammalian cell comprising the expression vector of claim 22.
- 24. (Original) The mammalian cell of claim 23, wherein said mammalian cell is a human cell.
- 25. (Canceled)
- 26. (Previously presented) The expression vector of claim 22, wherein said siRNA molecule comprises two distinct strands having complementary sense and antisense regions.
- 27. (Original) The expression vector of claim 22, wherein said siRNA molecule comprises a single strand having complementary sense and antisense regions.
- 28. (Withdrawn) A method of preventing, treating or alleviating NF-kappa-B dependent conditions in an individual, comprising administering a therapeutically effective amount of a

Axelsson and Good

Application No.: 10/582,946

Filed: March 2, 2007

Page 5

siRNA compound of claim 1, in a suitable pharmacological carrier so that expression of the p65 subunit of NF-kappa-B is suppressed, thereby suppressing NF-kappa-B dependent processes.

**PATENT** 

Atty Docket No.: INDEX1140-1

- 29. (Withdrawn) The method of claim 28, wherein the NF-kappa-B dependent condition is selected from cancer, cardiac disorders, ischaemia, and allergic/inflammatory diseases and conditions, wherein said allergic/inflammatory diseases and conditions are selected from the group consisting of asthma, allergic rhinitis, atopic dermatitis, psoriasis, rheumatoid arthritis, ulcerative proctits, ulcerative colitis, Crohn's disease and septic shock.
- 30. (Withdrawn) A method of preventing, treating or alleviating NF-kappa-B dependent conditions in an individual, comprising extracting cells, tissue or entire organs from said individual; contacting the said cells, tissue or entire organs with a siRNA molecule of claim 1, whereby expression of the p65 subunit of NF-kappa-B is suppressed, thereby suppressing NF-kappa-B dependent processes; and reintroducing the cells, tissues or organs back into said individual.
- 31. (Withdrawn) The method of claim 30, wherein said method is used as a step in a treatment involving a procedure selected from a group consisting of transplantation, graft, and implantation.